

Neil Scott Cutshall, Ph.D.

WORK ADDRESS

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SUMMARY

Scientific leader with a record of achievement in diverse drug discovery research environments. Skills include a strong background in synthetic organic and medicinal chemistry, and a working knowledge of biochemistry, biology and pharmacology related to drug discovery. Management experience includes project leadership, recruiting, and leading a group of B.S., M.S., and Ph.D. level scientists.

EMPLOYMENT HISTORY

Department of Chemistry, Omeros Corp., Seattle, Wash.
Director of Medicinal Chemistry, 2008-current

- Coordinating the medicinal chemistry for PDE10 and other CNS drug discovery programs.
- Directing external contract chemistry.
- Developed in house chemistry infrastructure and currently supervise a Ph.D. level chemist.
- Conducting synthetic chemistry.

Department of Chemistry, Omeros Corp., Seattle, Wash.
Sr. Group Leader, 2006-2008

- Project Leader for the PDE10 drug discovery project.
- Joint Program Advisory Committee representative and Program Coordinator with The Stanley Medical Research Institute.
- Coordinating the medicinal chemistry for PDE10 and other CNS drug discovery programs.
- Directing external contract chemistry.
- Developed in house chemistry infrastructure and currently supervise a Ph.D. level chemist.
- Conducting synthetic chemistry to better understand SAR of lead compounds.

Department of Chemistry, Nura Inc., Seattle, Wash.
Director of Medicinal Chemistry, 2005-2006

- Project Leader for PDE10 drug discovery.
 - Directed inhibitor design and synthesis.
 - Directed chemistry outsourcing.
 - Worked closely with in-house project team members from cellular biology, ADME/PK, and animal behavior departments to optimize inhibitors.
 - Led regular meetings with off-site project consultants and collaborators.

- Conducted medicinal chemistry outsourcing for other drug discovery programs.
- Drafted chemistry patents.

Department of Chemistry, Ceptry Inc., Bothell, Wash.
Group Leader, 2003-2005

- Group Leader within the Chemistry Department
 - Supervised a group of six Ph.D. and M.S. level reports.
 - Conducted weekly departmental chemistry meetings.
 - Participated in administration and budgeting duties.
 - Evaluated and acquired departmental equipment and software.
 - Headed recruitment activities for expansion of the chemistry department.
 - Participated in team planning and project training sessions.
 - Evaluated and purchased analytical instrumentation.
- Project Leader for the CDC14A drug discovery project
 - Worked closely with multiple departments including Discovery Biology, Biochemical Pharmacology, Cellular Pharmacology and High-Throughput Screening (HTS).
 - Managed critical path processes for the project including go/no go decisions, necessary staffing and assignments of tasks and timelines.
 - Organized and led regular project meetings.
 - Presented project reviews to Ceptry SAB and senior management.
- Chemistry core-team representative for the CDC14A project
 - Guided the medicinal chemistry efforts for 2 distinct inhibitor classes using structure-based drug design.
 - Personally carried-out chemistry to expand existing SAR.
 - Conducted external outsourcing of chemistry.

Department of Chemistry, Ceptry Inc., Bothell, Wash.
Senior Scientist, 2001-2003

- Medicinal chemistry core member of the JSP-1 drug discovery project.
- Designed and completed SAR on >150 targeted inhibitor analogs through the use of solution phase parallel synthetic strategies.
- Initiated outsourcing of targeted analogs with outside vendors. This included optimizing synthetic routes, selecting analogs for synthesis, receiving and submitting compounds for in-house biological testing and overseeing the appropriate documentation.
- Worked closely with the project team to establish critical path objectives.
- Presented project results to the SAB and senior Ceptry management.
- Initiated intellectual property protection for targeted classes of inhibitors. This included working with on-site and external legal council to draft provisional patents.
- Supervised a Research Associate.
- Maintained an active roll in the PTP1B project.
- Assisted in evaluating additional chemistry laboratory space for the company.
- Evaluated and coordinated the purchase and installation of a 400 MHz NMR.

Department of Chemical Genomics, Celltech R&D Inc., Bothell, Wash.
Senior Scientist, 2000-2001

- Promoted to Project Leader of Protocomics. Responsibilities included the

coordination of outside collaborators and the development of proprietary in-house proteomic tools toward the discovery of novel protein tyrosine phosphatases as well as other secreted and cell surface proteins.

- Synthesized and tested novel reagents for the selective labeling of specific protein classes.
- Directed a project team that included bioinformatics, expression profiling, computing, chemistry and in-house biology. Active in the evaluation of analytical instrumentation to conduct proteomic analyses.
- Supervised a Senior Research Associate.

Department of Chemistry, Celltech R&D Inc., Bothell, Wash.
Scientist II, 1998-2000

- Carried-out the design and synthesis of >350 novel small molecule CXCR2 chemokine receptor antagonists.
- Developed and conducted solid and solution phase parallel synthesis and purification techniques to rapidly expand SAR.
- Explored multiple compound series for *in vitro* potency and selectivity in a filter mat and SPA ligand binding, [³⁵S]GTPγS, calcium flux, and human neutrophil chemotaxis assays. A class of 6-alkylsulfanyl-nicotinanilides was optimized from 20 μM to 50 nM for selective receptor antagonism and functional inhibition of neutrophil chemotaxis.
- Designed and carried-out analytical studies to determine the chemical stability of selected compounds toward human plasma using HPLC-MS.
- Drafted provisional patents for selected compound series.

Department of Chemistry, Axyx Pharmaceuticals (Celera), South San Francisco, Calif.
Scientist, 1996-1998

- Synthesized >140 benzimidazole-based analogs and conducted SAR toward the development of small-molecule serine protease inhibitors.
- Initial research, in collaboration with Bayer AG, focused on the design and synthesis of potent and selective tryptase inhibitors. Successfully optimized second-generation inhibitors for oral bioavailability using novel non-charged P1 recognition elements and prodrug strategies.
- Conducted the synthesis of multi-gram quantities of selected compounds in support of preclinical studies.
- Presented regular research updates to senior management.
- Promoted to Hepatitis C Project Team Leader. Research was conducted in collaboration with Bristol-Myers Squibb. Multi-disciplinary responsibilities included designing and directing the medicinal chemistry for the project team, interfacing with the computational modeling group, and working closely with the biology project members.
- Hired and supervised the research of a Senior Research Associate.

Oregon State University, Corvallis, Ore.
Postdoctoral Research Associate (Professor James D. White), 1994-1996

- Completed the synthesis of (±)-euonyminol, the highly oxygenated sesquiterpenoid core of a cathedulin alkaloid.

Chemistry Department, ITT Rayonier Inc., Shelton, Wash.
Research Chemist, 1986-1989

- Responsibilities included independent research directed toward the molecular weight distribution of cellulose, supervision of research technicians, providing on-site assistance during mill trials, and installation of analytical instrumentation.
- Radiation safety officer, 1988-1989.

Battelle Northwest, Department of Energy, Richland, Wash.
Research Chemist, 1986

- Developed analytical techniques to monitor the autoxidation of coal.

Battelle Northwest, Department of Energy, Richland, Wash.
Chemistry Intern, 1985, Northwest College and University Association for Science (NORCUS)

- Examined how electric fields altered hormone levels in the pineal glands of rats.
- Investigated reaction mechanisms related to coal liquefaction processes.

EDUCATION

North Carolina State University, Raleigh, North Carolina
Ph.D. in Organic Chemistry (Professor R. J. Linderman), 1990-1994

- The formation of highly oxygenated tetrahydrofuran-3-one ring systems using an electrophilic carbonyl ylide synthon.
- Developed methodology was applied toward the asymmetric synthesis of (+)-breyndiolide.
- Research Assistant, 1991-1994
- Teaching Assistant, 1990-1991

Washington State University, Pullman, Wash.
B.S. in Chemistry (Professor Royston Filby, Research Advisor), 1984-1986

- Undergraduate research focused on the mechanism of deposition of titanium on coal liquefaction catalysts using instrumental neutron activation analysis.

PUBLICATIONS

- Cutshall, N.S.; O'Day, C.; Prezhdo, M. Rhodanine Derivatives as Inhibitors of JSP-1. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 3374-3379.
- O'Day, C.; Cutshall, N.S. Evidence That Cysteine 124 is Essential For Rhodanine Inhibition of JSP-1 Through a Covalent-Reversible Mechanism (manuscript in preparation).
- Cutshall, N.S.; Kucera, K.A.; Ursino, R.; Latham, J.; Ihle, N.C. Nicotinilides as Inhibitors of Neutrophil Chemotaxis. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 1517-1520.
- Cutshall, N.S.; Ursino, R.; Kucera, K.A.; Latham, J.; Ihle, N.C. Nicotinamide *N*-Oxides as CXCR2 Antagonists. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 1951-1954.
- White, J.D.; Shin, H.; Kim, T.-S.; Cutshall, N.S. Total Synthesis of the Sesquiterpenoid Polyols (±)-Euonyminol and (±)-3,4-Dideoxymaytol, Core Constituents of the Esters of the *Celastraceae*. *J. Am. Chem. Soc.* **1997**, *119*, 2404-2419.
- White, J.D.; Cutshall, N.S.; Kim, T.-S.; Shin, H. Total Synthesis of (±)-

Euonyminol, the Sesquiterpenoid Nucleus of Cathedulin K-19, via an Epoxide Cascade Cyclization. *J. Am. Chem. Soc.* **1995**, *117*, 9780-9781.

- Linderman, R.J.; Cutshall, N.S.; Becicka, B.T. Synthesis of Tetrahydrothiophenes Via Nucleophilic Addition of Harpp's Reagent to Cyclic Carbonates: Application Toward the Synthesis of Breynolide. *Tetrahedron Lett.* **1994**, *35*, 6639-6642.

PRESENTATIONS

- Neil S. Cutshall, Nathan C. Ihle, Kristin A. Kucera, Rocky Ursino, and John Latham, "Synthesis and SAR Studies of Nicotinamide N-Oxides as CXCR2 and CXCR1 Antagonists," American Chemical Society 222nd National Meeting, Chicago, IL, MEDI-266, August 26-30, 2001.
- Neil S. Cutshall, James D. White, Tae-Seong Kim, Hyunuk Shin, "Total Synthesis of (±)-Euonyminol," American Chemical Society 51st Northwest Regional Meeting, Corvallis, OR, #140, June 19-22, 1996.
- James D. White, Hyunuk Shin, Tae-Seong Kim, Neil S. Cutshall, "The Synthesis of (±)-Euonyminol," 34th National Organic Symposium, Williamsburg, VA, #92, June 11-15, 1995.
- R.J. Linderman, N.S. Cutshall, "Asymmetric Synthesis of the Tetrahydrothiophene Portion of Breynolide," American Chemical Society 46th Southeast Regional Meeting, Birmingham, AL, #334, October 16-19, 1994.
- R.J. Linderman, N.S. Cutshall, W.R. Kwochka, "Progress Toward the Asymmetric Syntheses of (+)-Breynolide and (+)-Phyllanthocin," American Chemical Society 206th National Meeting, Chicago, IL, ORGN-426, August 23-27, 1993.
- N.S. Cutshall, B.T. Becicka, R.J. Linderman, "Progress Toward Breynolide via an Electrophilic Carbonyl Ylide Synthon Approach," American Chemical Society 204th National Meeting, Washington, D.C., ORGN-327, August 23-28, 1992.
- R.J. Linderman, W. Kwochka, N.S. Cutshall, B.T. Becicka, B. Miburo, "Oxacycle Synthesis via an Electrophilic Carbonyl Ylide Synthon," American Chemical Society 44th Southeastern-26th Middle Atlantic Regional Meeting, Arlington, VA, #142, December 6-9, 1992.
- N.S. Cutshall, B.T. Becicka, R.J. Linderman, "Approaches to Breynolide," American Chemical Society 106th North Carolina Sectional Conference, University of North Carolina, Chapel Hill, NC, April 4, 1992.

PATENTS

- "Compounds and methods for regulating protein tyrosine phosphatases." Cutshall, Neil S. Provisional.
- "Pharmaceutical Uses and Synthesis of nicotinilide-N-oxides." Cutshall, Neil S.; Yager, Craig M. US 7,141,590.
- "Pharmaceutical uses and synthesis of nicotinamides." Cutshall, Neil S.; Jeffrey, Scott C. US 7,151,112.
- "Preparation of 3-acylaminopyridine and nicotinamide derivatives as antiinflammatory agents." Cutshall, Neil S.; Jeffrey, Scott C. US 6777432.
- "Preparation of nicotinilide-N-oxides as G-protein-coupled receptor antagonist for the treatment of inflammation due to neutrophil chemotaxis." Cutshall, Neil S.; Yager, Craig M. WO 2002053544.
- "Preparation of compounds and compositions for treating diseases associated with serine protease, particularly tryptase, activity." Church, Timothy J.; Cutshall, Neil S.; Gangloff, Anthony, R.; Jenkins, Thomas, E.; Linsell, Martin, S.; Litvak, Joane; Rice, Kenneth, D.; Spencer, Jeffrey, R. WO 9845275.

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| CONSULTING | <ul style="list-style-type: none"> • Davis Wright Tremaine LLP, Seattle, Wash. |
| REFEREED JOURNALS | <ul style="list-style-type: none"> • Journal of Organic Chemistry • Bioorganic and Medicinal Chemistry Letters • Tetrahedron Letters |
| AWARDS AND HONORS | <ul style="list-style-type: none"> • North Carolina State University Organic Chemistry Graduate Award, 1994. • Burroughs Wellcome Fellow in Synthetic Organic Chemistry, 1991-1992. • Washington State University Chemistry Alumni Undergraduate Scholarship, 1985. • Hanford Environmental Health Foundation Board of Trustees Scholarship, 1982. • Eagle Scout, 1982. |
| MEMBERSHIP | <ul style="list-style-type: none"> • Phi Lambda Upsilon, President, 1992-1993; Alumni Secretary, 1993-1994. • American Chemical Society; Organic and Medicinal Chemistry Division Member. • Toastmasters International, 1987-1989; Secretary-Treasurer, 1987-1988. |
| REFERENCES | <ul style="list-style-type: none"> • Available upon request. |